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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/764,604 | 01/27/2004 | Karen McLachlan | 2159.0030001/LBB/PAC | 6570 |

26111 7590 09/14/2006

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WASHINGTON, DC 20005

| EXAMINER | |
|---|---|
| YAO, LEI | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1642 | |

DATE MAILED: 09/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/764,604 | MCLACHLAN ET AL. | |
| | Examiner | Art Unit | |
| | Lei Yao, Ph.D. | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *1-8, 19-31, 34-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-18, 32, 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/10/04, 1/20/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *exhibit*.

## DETAILED ACTION

### *RESPONSE TO ARGUMENTS*

The Amendment filed on 6/22/06 in response to the previous Non-Final Office Action (2/03/06) is acknowledged and has been entered.

Claims 9, 10, 33 have been amended. Claims 1-43 are pending. Claims 1-8, 19-31 and 34-43 have been withdrawn previously for non-elected invention. Claims 9-18, 32 and 33 are under consideration.

**The text of those sections of Title 35, U.S.Code not included in this action can be found in the prior Office Action.**

**The following office action contains NEW GROUNDS of rejection.**

It is noted that the claims 10, 12 and 33 have been amended to add new species presented in a Markush group. However, the species in the amended claims are not originally presented, which may be subjected to the restriction/election requirement in the process of future prosecution.

***Information Disclosure Statement***

The information disclosure statement (s) (IDS) submitted on 11/10/04 and 1/20/06 are/is considered by the examiner and initialed copies/copy of the PTO-1449 are/is enclosed.

***Rejections Withdrawn***

1. The rejection of claims 9, 12-18 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for term "associate with IGSF9" is withdrawn in view of the amendments to the claims reciting antibody or antigen binding fragment which binds to IGSF9.

2. The rejection of claims 9-18 and 32-33 under 35 U.S.C. 102(b) as being anticipated by Hoefnagel et al., (Eur J Nucl Med, vol 28, page 359-68, 2001) is withdrawn in view of the amendments to the claims.

3. The rejection of claims 9-11 and 32 under 35 U.S.C. 112 first paragraph, as failing to comply with the enablement requirement is withdrawn in view of the amendments to the claims. The rejection of the other claims under 35 U.S.C. 112 first paragraph in prior office action is maintained (see below).

***Response to Arguments***

***Rejection under 35 USC § 112 1st paragraph***

***Drawn to enablement***

The rejection of claims 12-18 and 33 under 35 U.S.C. 112 first paragraph, as failing to comply with the enablement requirement is maintained for the reasons of record in the prior Office Action (2/23/06) and state again for the newly amended claims 12, 18, and 33 below.

> Claims are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.
>
> Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.
>
> The claims are drawn to a method of treating a mammal exhibiting a neoplastic disorder comprising administering an antibody or antigen binding fragment comprising domain deleted anti-IGSF9 that is associated with IGSF9 (referred as SEQ ID NO: 2, page 7 of instant specification or para 30). To satisfy the requirement of 112, 1st paragraph, it is necessary that the specification provide an enabling disclosure of how to make and use a claimed invention. The method objective of claims is a method of treating a cancer with antigen binding fragment comprising an antibody to IGSF9. Thus, it would be expected that one of skill in the art would be able to treat a neoplastic disorder comprising a cancer with any antibody comprising any domain deleted antibodies to IGSF9 without undue experimentation by using the claimed method.
>
> The specification teaches a method of generating a monoclonal anti-IGSF9 antibody (see pages 93-94). The specification teaches a general method of treating cancer and states that based on analysis of the levels of IGSF9 in tumor sample a treatment regime determined using acceptable treatment alternative known to those skilled in the art. However, the specification does not provide a method of treating any cancer with any agent, which could bind to IGSF9 comprising any antibody to IGSF9 (SEQ ID NO: 2). Thus, the specification invites the skilled artisan to experiment to determine how to use the claimed antibody to IGSF9 and does not set forth sufficient teachings to allow one skilled in the art to practice treating a neoplastic disorder including a cancer. There are no working examples to guide or assist the skilled artisan in practicing the claimed method of treating any neoplastic disorder with antibody or binding fragment to IGSF9.
>
> The instant specification provides insufficient guidance or direction to predictably enable one of ordinary skill in the art to use the invention as claimed. Those of skill in the art recognize the unpredictability of treating tumors with antibodies. For example, Jain R. K. (Scientific American, 271(1): 58-65, July 1994) discloses the art known barriers to the delivery of drugs into solid tumors. These impediments include (1) Non-uniform blood delivery to all areas of the tumor in which some areas of the tumor receive therapeutic agents and other areas of the tumor receive no therapeutic agent at all. (Page 60 col. 3); (2) Increased viscosity of blood in the tumor itself which also hinders drug delivery to the tumor (see paragraph bridging pages 60 and 61); (3) High liquid pressures in the interstitial matrix can retard the delivery of large therapeutic agents, such as antibodies, into tumors (page 61, Col. 1 paragraph 1); (4) Convection is a necessary mechanism by which larger therapeutic molecules such as antibodies, reach target cells which are not directly fed by the vasculature. Convection is not observed in large tumors (defined as more than ½ centimeter in diameter, page 62 col. 1) and convection is necessary for adequate drug delivery of molecules having a molecular weight of more than 5000 (page 61, col. 1 through page 63, col. 3) and (4) Molecules as large as antibodies (i.e., MW=150,000) would require several months to reach a uniform concentration in a tumor that measures 1 centimeter in radius (page 63, col. 2). Further, Dillman R. O., (Annals of Internal Medicine, 111:592-603, 1989) summarizes (see abstract) the status of in-vivo use of monoclonal antibodies for treating cancer wherein despite advances in biotechnology, many major hurdles persist including tumor cell heterogeneity, lack of cytotoxicity, and the development of human anti-mouse antibodies (HAMA). Also,

Weiner L. M. (Seminars in Oncology, 26 (4 Suppl 12): 41-50, August 1999) provided an overview of monoclonal antibody therapy including some promising activity, however, major obstacles to clinical efficacy still exist extending the unpredictability of this treatment. This includes impaired distribution and delivery of antibody to the tumor site, inadequate trafficking of potential cellular effectors to tumor, antigenic heterogeneity, shed or internalized targets and insufficient target specificity (see page 43).

Furthermore, as disclosed by Dillman, R. O. (Journal of Clinical Oncology, 12(7):1497-1515, 1994) discloses, after reviewing the literature on the use of unconjugated monoclonal antibodies to treat cancer, that "at present, there are no unconjugated monoclonal antibodies that have proven therapeutic benefit in hematologic malignancies or solid tumors." Thus, absent objective evidence to the contrary, it is highly unpredictable that applicant's unconjugated antibody would possess any therapeutic effects.

Baughn et al (WO2003051902, filed 5/31/02) teach that a protein, which is 100% identical to the amino acid sequence of SEQ IDNO: 2 (referred to IGSF9, instant specification, page 7 or para 30) is neurotransmitter (see abstract and exhibit A). Thus, absent objective evidence to the contrary, it is highly unpredictable that claimed binding fragment or antibodies that bind IGSF9 would possess any therapeutic effect for just any neoplastic disorder comprising cancer.

No direction or guidance is provided in current specification to assist one skilled in the art using a binding fragment or antibody that binds IGSF9 (SEQ ID NO: 2) in a method of treating neoplastic disorder in a mammal. In view of the lack of the predictability of the art to which the invention pertains as evidenced by the art of Jain R. K., Dillman R. O. (Weiner L. M., Dillman J., Satyamoorthy et al and Lehmann et al, and the lack of established clinical protocols for effective immunotherapy, one skilled in the art would be forced into under experimentation in order to practice the claimed invention.

The response filed 6/22/06 has been carefully considered but is deemed not to be persuasive. The response states that experiments have been performed identifying which types of tumor have increased expression of IGSF9 and the specification described the preparation of a monoclonal antibody hat specifically binds to IGSF9 expressed on the tumor sample (page 11-12). In response to this argument, Applicants are claiming a method of treating a mammal by administering antibody to IGSF9, not detecting IGSF9 on tumor cells or diagnosing a tumor by expression of the IGSF9 protein. Thus, under 35 U.S.C. 112 first paragraph, Applicants need to provide enabled method for one skilled in the art to in order to practice the claimed invention of treating neoplastic disorder comprising the cancers with antibody or antigen binding fragment to IGSF9 without undo experimentation. However, the instant specification, on page 102-103, example 8, describes a method of treating cancer and states " *base on analysis of the level of IGSF9 in tumor sample, a treatment regime is determined using acceptable treatment alternative know to those skilled in the art*" and " *knowledge of the IGSF9 expression in primary tumor at the time of diagnosis and surgical removal may therefore directly influence therapeutic decisions*", also states "*knowledge of IGSF9 levels may be useful for application of new cancer therapies*". The specification does not provide a working example how the cancers were treated and what the result of the treatment. Basically, the specification invites the skilled artisan to experiments to

test claimed antibody to IGSF9 for cancer treatment without knowing whether the method are working or not. The specification does not provide sufficient teachings to allow one skilled in the art to practice treating a neoplastic disorder including a cancer. There are no working examples to guide or assist the skilled artisan in practicing the claimed method of treating any neoplastic disorder with antibody or binding fragment to IGSF9. The applicants further argue that the examiner provide several articles, which are not representative of the state of the art of present invention. In response to this argument, the problems of antibody treatments in the art stated in the reference have not been overcome currently. One skilled in the art will not convinced to practice the claimed method for treating cancer until the result of experimentation is provided by applicants because of unpredictability of claimed method. Again, as stated by Weiner (seminars in oncology), for the monoclonal antibody therapy, major obstacles to clinical efficacy still exist extending the unpredictability of this treatment. Since the unpredictability of the treatment method in the cancer, since no direction and guideline provided by applicants as well as one skilled in the art for the cancer treatment with antibody to IGSF9 (art teaches that IGSF9 protein is a neuron transmitter) and since no working example for the treatment provided by applicants, one skilled in the art would be forced into under experimentation in order to practice the claimed invention. If Applicants has any objective evidence contrary to the rejection, Applicant is invited to submit it to the Office for reconsideration

***The following is a New Ground of rejection-based on the amendment to the claims***

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 9 is rejected under 35 U.S.C. 102(e) as being anticipated by Afar et al., (WO2003042661, effective filing date 11/13/2001).

Claim 9 is drawn to a composition comprising an antibody or antigen binding fragment to IGSF9.

Afar et al., disclose a composition comprising an antibody binding to a protein, which is 100% identical to IGSF9 protein in amino acid sequence (SEQ ID NO: 2) as evidenced by protein sequence search (exhibit, page 48).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquires set forth in Graham V. john Deere Co., 383 U.S. 1, 148 USPQ 459 (1996), that are applied for establishing a background for determining obviousness under 25 U.S. C. 103 (a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or obviousness

Claims 9-11, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Afar et al., (WO2003042661, effective filing date 11/13/2001) in view of Chinn et al., (US patent 699840, effective filing date Jul 28, 2000).

Claim 9 is set forth above. Claims 10-11 are further drawn to the antibody to IGSF9 protein linked to a bifunctional chelators, MX-DTPA and CHX-DTPA. Claim 32 is drawn to a kit comprising the composition of claim 9.

Afar et al., disclose antibody to the IGSF9 protein.

Afar et al., do not disclose that the antibody is linked to bifunctional chelators and not disclose a kit comprising an antibody to the IGSF9 protein.

Chinn et al., teach a method of linking an antibody to bifunctional chelators MX-DTPA and CHX-DTPA, which let antibody effectively bind to radioisotope of interest. Chinn et al., also teach a kit comprising the antibody as an active component (col 7 and entire patent).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to link the antibody with a bifunctional chelator to have the advantage of the binding of antibody to both protein and radioisotope for cancer treatment. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a kit including the necessary reagents to perform an assay in a kit format for the convenience and economy of the user. One would have been motivated with a reasonable expectation of success to link the chelators MX-DTPA and CHX-DTPA with the antibody IGSF9 protein and the assemble the reagents in a kit format to standardize the reagents for the optimization the assay for use in a clinical use because Afar et al., have shown an antibody to IGSF9 protein, which can be used for detecting or blocking activity of the IGSF9 and Chinn et al., have shown the method of forming a kit and making an antibody linked to bifunctional chelator, MX-DTPA and CHX-DTPA.

***Conclusion***

NO claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao, Ph.D.
Examiner
Art Unit 1642

LY

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER

GenCore version 5.1.7


OM protein - protein search, using sw model

Run on: February 3, 2006, 22:37:29 ; Search time 205 Seconds
(without alignments)
2492.671 Million cell updates/sec

Title: US-10-764-604-2
Perfect score: 6163
Sequence: 1 MVWCLGLAVLSLVISQGADG.....RARLPAYRQPVPHPEQATLL 1163

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 2443163 seqs, 439378781 residues

Total number of hits satisfying chosen parameters: 2443163

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_21:*
1: geneseqp1980s:*
2: geneseqp1990s:*
3: geneseqp2000s:*
4: geneseqp2001s:*
5: geneseqp2002s:*
6: geneseqp2003as:*
7: geneseqp2003bs:*
8: geneseqp2004s:*
9: geneseqp2005s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

| Result No. | Score | % Query Match | Length | DB | ID | Description |
|---|---|---|---|---|---|---|
| 1 | 6163 | 100.0 | 1163 | 7 | ADN39938 | Adn39938 Cancer/an |
| 2 | 6163 | 100.0 | 1163 | 8 | ADR28007 | Adr28007 Human imm |
| 3 | 6163 | 100.0 | 1163 | 8 | ADR28015 | Adr28015 Short for |
| 4 | 6163 | 100.0 | 1163 | 8 | ADR46652 | Adr46652 Cancer-as |
| 5 | 6153 | 99.8 | 1163 | 8 | ADR28016 | Adr28016 Consensus |
| 6 | 6138 | 99.6 | 1163 | 7 | ADE28117 | Ade28117 Human NTR |
| 7 | 6117 | 99.3 | 1179 | 5 | ABB97578 | Abb97578 Novel hum |
| 8 | 6117 | 99.3 | 1179 | 8 | ADR28014 | Adr28014 Long form |
| 9 | 6117 | 99.3 | 1179 | 8 | ADR28013 | Adr28013 Long form |
| 10 | 3809 | 61.8 | 953 | 8 | ADR28009 | Adr28009 Short for |
| 11 | 3780 | 61.3 | 969 | 8 | ADR28011 | Adr28011 Long form |
| 12 | 3557.5 | 57.7 | 798 | 6 | ABJ20228 | Abj20228 Human IG |
| 13 | 2004 | 32.5 | 1353 | 8 | ADS98072 | Ads98072 Protein f |
| 14 | 1955 | 31.7 | 1426 | 5 | ADH48822 | Adh48822 NOV45A pr |
| 15 | 1940.5 | 31.5 | 1356 | 5 | ADH48824 | Adh48824 NOV45B pr |
| 16 | 1722 | 27.9 | 325 | 8 | ADK00609 | Adk00609 HOMO prot |
| 17 | 1542 | 25.0 | 340 | 3 | AAY76006 | Aay76006 Murine Ig |
| 18 | 1542 | 25.0 | 340 | 4 | AAB55945 | Aab55945 Skin cell |
| 19 | 1542 | 25.0 | 340 | 5 | ABB72145 | Abb72145 Murine pr |
| 20 | 1396.5 | 22.7 | 600 | 7 | ADM05772 | Adm05772 Human pro |
| 21 | 648 | 10.5 | 142 | 8 | ADR28027 | Adr28027 Murine lo |
| 22 | 648 | 10.5 | 142 | 8 | ADR28028 | Adr28028 Murine Ov |
| 23 | 605 | 9.8 | 871 | 4 | AAM78479 | Aam78479 Human pro |
| 24 | 605 | 9.8 | 871 | 4 | AAM79463 | Aam79463 Human pro |
| 25 | 605 | 9.8 | 871 | 8 | ADS98675 | Ads98675 Protein f |
| 26 | 542 | 8.8 | 400 | 4 | ABB70599 | Abb70599 Drosophil |
| 27 | 540.5 | 8.8 | 694 | 4 | ABB70601 | Abb70601 Drosophil |
| 28 | 531 | 8.6 | 1386 | 8 | ABO84548 | Abo84548 Human can |
| 29 | 494.5 | 8.0 | 1372 | 8 | ABO84547 | Abo84547 Mouse can |
| 30 | 467 | 7.6 | 89 | 5 | ABB53111 | Abb53111 Human ORF |
| 31 | 456 | 7.4 | 1447 | 2 | AAR68553 | Aar68553 Deleted i |
| 32 | 456 | 7.4 | 1447 | 2 | AAY33498 | Aay33498 Human DCC |
| 33 | 456 | 7.4 | 1447 | 4 | AAB50693 | Aab50693 Human UNC |
| 34 | 456 | 7.4 | 1447 | 6 | ABJ19765 | Abj19765 Human MP2 |
| 35 | 456 | 7.4 | 1447 | 9 | AEB93526 | Aeb93526 Human del |
| 36 | 454.5 | 7.4 | 3931 | 6 | ABU07377 | Abu07377 Human pro |
| 37 | 454.5 | 7.4 | 3931 | 7 | ADG39786 | Adg39786 Human nov |
| 38 | 453.5 | 7.4 | 1380 | 8 | ADM32911 | Adm32911 Amino aci |
| 39 | 453.5 | 7.4 | 1394 | 8 | ABO84683 | Abo84683 Human can |
| 40 | 453.5 | 7.4 | 1396 | 8 | ABO84684 | Abo84684 Human can |
| 41 | 453 | 7.4 | 1612 | 9 | ADX83222 | Adx83222 Human TEG |
| 42 | 453 | 7.4 | 1651 | 2 | AAY13566 | Aay13566 Human Rob |
| 43 | 453 | 7.4 | 1651 | 6 | ABU04093 | Abu04093 Human exp |
| 44 | 453 | 7.4 | 1651 | 6 | ABU04089 | Abu04089 Human exp |
| 45 | 453 | 7.4 | 1651 | 6 | ABU04094 | Abu04094 Human exp |

ALIGNMENTS

RESULT 1
ADN39938
ID ADN39938 standard; protein; 1163 AA.
XX
AC ADN39938;
XX
DT 17-JUN-2004 (first entry)
XX
DE Cancer/angiogenesis/fibrosis-related polypeptide, SEQ ID NO:C308.
XX
KW Human; differential expression; cancer; angiogenic disorder;
KW fibrotic disorder; psoriasis; ischaemia; heart disease; atherosclerosis;
KW inflammatory disease; autoimmune disease;
KW retinal neovascularistaion syndrome; scarring; uterine fibroid;
KW detection; diagnosis; prognosis; drug screening; drug targeting;
KW wound healing; contraception; cytostatic; cardiant; immunomodulatory;
KW vulnerary; gene therapy; vaccine.
XX
OS Homo sapiens.
XX
PN WO2003042661-A2.
XX
PD 22-MAY-2003
XX
PF 13-NOV-2002; 2002WO-US036810.
XX
PR 13-NOV-2001; 2001US-0350666P.
PR 21-NOV-2001; 2001US-0332464P.
PR 29-NOV-2001; 2001US-0334393P.
PR 03-DEC-2001; 2001US-0335394P.
PR 14-DEC-2001; 2001US-0340376P.
PR 08-JAN-2002; 2002US-0347211P.
PR 10-JAN-2002; 2002US-0347349P.
PR 08-FEB-2002; 2002US-0355250P.
PR 13-FEB-2002; 2002US-0356714P.
PR 20-FEB-2002; 2002US-0359077P.
PR 29-MAR-2002; 2002US-0368809P.
PR 04-APR-2002; 2002US-0370110P.
PR 12-APR-2002; 2002US-0372246P.
PR 05-JUN-2002; 2002US-0386614P.
PR 16-JUL-2002; 2002US-0396839P.
PR 22-JUL-2002; 2002US-0397775P.
PR 22-JUL-2002; 2002US-0397845P.
PR 09-SEP-2002; 2002US-0409450P.
XX
PA (EOSB-) EOS BIOTECHNOLOGY INC.
XX

Exhibit

PI Afar D, Aziz N, Ginsburg WM, Gish KC, Glynne R, Hevezi PA;
PI Mack DH, Murray R, Watson SR, Wilson KE, Zlotnik A;
XX
DR WPI; 2003-468649/44.
DR N-PSDB; ADN39721.
XX
PT Determining the presence or absence of a pathological cell in a patient,
PT useful for diagnosing, prognosing or treating cancer, comprises detecting
PT a nucleic acid in a biological sample.
XX
PS Claim 12; SEQ ID NO C308; 1385pp; English.
XX
CC The invention relates to nucleic acids and proteins (ADN38683-ADN40064)
CC whose expression is upregulated or downregulated in specific cancers or
CC other diseases such as angiogenic or fibrotic disorders, and to methods
CC of determining the presence or absence of a pathological cell in a
CC patient by detecting a nucleic acid at least 80% identical to those of
CC the invention or by detecting a polypeptide of the invention. The
CC invention also relates to expression vectors and host cells comprising a
CC nucleic acid of the invention; antibodies which specifically bind a
CC polypeptide of the invention; use of such antibodies for drug targeting;
CC and methods of screening for modulators of activity or expression of the
CC polypeptides and nucleic acids. The nucleic acids, polypeptides,
CC antibodies and methods are useful for diagnosing, prognosing and treating
CC cancer and other conditions such as psoriasis, ischaemia, heart disease,
CC atherosclerosis, inflammatory diseases, autoimmune diseases, retinal
CC neovascularistaion syndromes, scarring and uterine fibroids. They may
CC also be useful in wound healing and in contraception. The present
CC sequence represents a polypeptide of the invention.
XX
SQ Sequence 1163 AA;

Query Match 100.0%; Score 6163; DB 7; Length 1163;
Best Local Similarity 100.0%; Pred. No. 0;
Matches 1163; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy    1 MVWCLGLAVLSLVISQGADGRGKPEVVSVVGRAEESVVLGCDLLPPAGRPPLHVIEWLRF 60
Db    1 MVWCLGLAVLSLVISQGADGRGKPEVVSVVGRAEESVVLGCDLLPPAGRPPLHVIEWLRF 60

Qy   61 GFLLPIFIQFGLYSPRIDPDYVGRVRLQKGASLQIEGLRVEDQGWYECRVFFLDQHIPED 120
Db   61 GFLLPIFIQFGLYSPRIDPDYVGRVRLQKGASLQIEGLRVEDQGWYECRVFFLDQHIPED 120

Qy  121 DFANGSWVHLTVNSPPQFQETPPAVLEVQELEPVTLRCVARGSPLPHVTWKLRGKDLGQG 180
Db  121 DFANGSWVHLTVNSPPQFQETPPAVLEVQELEPVTLRCVARGSPLPHVTWKLRGKDLGQG 180

Qy  181 QGQVQVQNGTLRIRRVERGSSGVYTCQASSTEGSATHATQLLVLGPPVIVVPPKNSTVNA 240
Db  181 QGQVQVQNGTLRIRRVERGSSGVYTCQASSTEGSATHATQLLVLGPPVIVVPPKNSTVNA 240

Qy  241 SQDVSLACHAEAYPANLTYSWFQDNINVFHISRLQPRVQILVDGSLRLLATQPDDAGCYT 300
Db  241 SQDVSLACHAEAYPANLTYSWFQDNINVFHISRLQPRVQILVDGSLRLLATQPDDAGCYT 300

Qy  301 CVPSNGLLHPPSASAYLTVLCMPGVIRCPVRANPPLLFVSWTKDGKALQLDKFPGWSQGT 360
Db  301 CVPSNGLLHPPSASAYLTVLCMPGVIRCPVRANPPLLFVSWTKDGKALQLDKFPGWSQGT 360

Qy  361 EGSLIIALGNEDALGEYSCTPYNSLGTAGPSPVTRVLLKAPPAFIERPKEEYFQEVGREL 420
Db  361 EGSLIIALGNEDALGEYSCTPYNSLGTAGPSPVTRVLLKAPPAFIERPKEEYFQEVGREL 420

Qy  421 LIPCSAQGDPPPVVSWTKVGRGLQGQAQVDSNSSLILRPLTKEAHGHWECSASNAVARVA 480
Db  421 LIPCSAQGDPPPVVSWTKVGRGLQGQAQVDSNSSLILRPLTKEAHGHWECSASNAVARVA 480

Qy  481 TSTNVYVLGTSPHVVTNVSVVALPKGANVSWEPGFDGGYLQRFSVWYTPLAKRPDRMHHD 540
Db  481 TSTNVYVLGTSPHVVTNVSVVALPKGANVSWEPGFDGGYLQRFSVWYTPLAKRPDRMHHD 540

Qy  541 WVSLAVPVGAAHLLVPGLQPHTQYQFSVLAQNKLGSGPFSEIVLSAPEGLPTTPAAPGLP 600
Db  541 WVSLAVPVGAAHLLVPGLQPHTQYQFSVLAQNKLGSGPFSEIVLSAPEGLPTTPAAPGLP 600

Qy  601 PTEIPPPLSPPRGLVAVRTPRGVLLHWDPPELVPKRLDGYVLEGRQGSQGWEVLDPAVAG 660
Db  601 PTEIPPPLSPPRGLVAVRTPRGVLLHWDPPELVPKRLDGYVLEGRQGSQGWEVLDPAVAG 660

Qy  661 TETELLVPGLIKDVLYEFRLVAFAGSFVSDPSNTANVSTSGLEVYPSRTQLPGLLPQPVL 720
Db  661 TETELLVPGLIKDVLYEFRLVAFAGSFVSDPSNTANVSTSGLEVYPSRTQLPGLLPQPVL 720

Qy  721 AGVVGGVCFLGVAVLVSILAGCLLNRRRAARRRRKRLRQDPPLIFSPTGKSAAPSALGSG 780
Db  721 AGVVGGVCFLGVAVLVSILAGCLLNRRRAARRRRKRLRQDPPLIFSPTGKSAAPSALGSG 780

Qy  781 SPDSVAKLKLQGSPVPSLRQSLLWGDPAGTPSPHPDPPSSRGPLPLEPICRGPDGRFVMG 840
Db  781 SPDSVAKLKLQGSPVPSLRQSLLWGDPAGTPSPHPDPPSSRGPLPLEPICRGPDGRFVMG 840

Qy  841 PTVAAPQERSGREQAEPRTPAQRLARSFDCSSSSPSGAPQPLCIEDISPVAPPPAAPPSP 900
Db  841 PTVAAPQERSGREQAEPRTPAQRLARSFDCSSSSPSGAPQPLCIEDISPVAPPPAAPPSP 900

Qy  901 LPGPGPLLQYLSLPFFREMNVDGDWPPLEEPSPAAPPDYMDTRRCPTSSFLRSPETPPVS 960
Db  901 LPGPGPLLQYLSLPFFREMNVDGDWPPLEEPSPAAPPDYMDTRRCPTSSFLRSPETPPVS 960

Qy  961 PRESLPGAVVGAGATAEPPYTALADWTLRERLLPGLLPAAPRGSLTSQSSGRGSASFLRP 1020
Db  961 PRESLPGAVVGAGATAEPPYTALADWTLRERLLPGLLPAAPRGSLTSQSSGRGSASFLRP 1020

Qy 1021 PSTAPSAGGSYLSPAPGDTSSWASGPERWPRREHVVTVSKRRNTSVDENYEWDSEFPGDM 1080
Db 1021 PSTAPSAGGSYLSPAPGDTSSWASGPERWPRREHVVTVSKRRNTSVDENYEWDSEFPGDM 1080

Qy 1081 ELLETLHLGLASSRLRPEAETELGVKTPEEGCLLNTAHVTGPEARCAALREEFLAFRRRR 1140
Db 1081 ELLETLHLGLASSRLRPEAETELGVKTPEEGCLLNTAHVTGPEARCAALREEFLAFRRRR 1140

Qy 1141 DATRARLPAYRQPVPHPEQATLL 1163
Db 1141 DATRARLPAYRQPVPHPEQATLL 1163
```

RESULT 2
ADR28007
ID ADR28007 standard; protein; 1163 AA.
XX
AC ADR28007;
XX
DT 04-NOV-2004 (first entry)
XX
DE Human immunoglobulin superfamily, member 9 (IGSF9) protein.
XX
KW Antibody; IGSF9; immunoglobulin superfamily member 9; LIV-1;
KW neoplastic disorder; vaccine; anti-idiotypic; cancer; antisense therapy;
KW cytostatic.
XX
OS Homo sapiens.
XX
PN WO2004066933-A2.
XX
PD 12-AUG-2004.
XX
PF 27-JAN-2004; 2004WO-US002044.
XX
PR 27-JAN-2003; 2003US-0442535P.
XX
PA (MCLA/) MCLACHLAN K.
PA (GLAS/) GLASER S.
PA (PEAC/) PEACH R J.
PA (ROWE/) ROWE T.
XX